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Application of the Forgotten Effects Model to the Economic Effects for Public European Health Systems by the Early Diagnostics of Emergent and Rare Diseases

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Abstract

The development of new, evidence-based treatments relies on an improved understanding of the often very complex pathophysiology of diseases. The systems (bio) medicine approaches have the potential to tackle this complexity through the integration of a variety of biological and medical research data and computational modelling. A European collaborative approach is required to assemble the necessary multidisciplinary expertise (e.g. biology, medicine, mathematics, computational technologies, and economics) to implement these last systems, which are approached in order to reduce the cost of the European Public Health System and simultaneously improve the wellbeing among citizens.

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Keywords:

1. Introduction

The main objective of our proposal is to emphasize and quantify the economic benefits that the early detection and treatment of rare and emergent diseases has on the European countries and society in general. Rare and emergent diseases (REDs) are the group of diseases that are not investigated properly due to the lack of information

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and the small percentage of the population suffering them. Medical experts, vanguard computational engineering and a robust set of economic models will be combined in order to create improved medical diagnostics, an innovative decision making software intended primarily for practitioners and to precisely quantify the positive economic impacts that such efforts represent for European public health systems, searching for scalability to other diseases.

2. Materials and methods

We suggest a methodology managed to know the cause-effect relations that remain hidden when doing a causality study between different elements [6-7]. We will start our approach with an uncertain cause-effect matrix defined by two groups of elements:

$A = \{a_i / i = 1,2,..., n\}$, which act as causes

$B = \{b_j / j = 1,2,..., m\}$, which act as effects

In addition, a causality relation [M] defined by the matrix:

$[M] = \{\mu_{a_i b_j} \in [0, 1] / i = 1,2,..., n; j = 1,2,..., m\}$ being $\mu_{a_i b_j}$ the characteristic pertinence relations from every single element of the matrix [M] (formed by the rows corresponding to the elements from de group A –causes- and the columns corresponding to the elements from the group B –effects). We could say, then, that the matrix [M] is composed by the estimations formed around all the effects where the elements from the group A exercise over the elements from the group B. The more meaningful this incidence relation is, the higher the value of each of the elements of the matrix will be. In this case, as we have departed from the fact that the characteristic pertinence relation had to take part in the interval [0, 1], we understand that the higher the incidence relation is, the nearer to 1 the assigned value will result. We must emphasize the fact that this initial matrix [M] is elaborated departing from the direct cause-effect relations, in other words, from the first generation. Our aim is based on obtaining a new incidence matrix, but reflecting not only the direct causalities, but also the ones, which, even though not being evident, still exist and are sometimes vital to appreciate certain facts. For this reason, it's necessary to build two additional incidence relations, which will pick up the possible effects which will come from deriving causes between causes (ion one hand) and effects between effects (on the other hand).

These two auxiliary matrixes are defined as:

$$[A] = \{\mu_{a_i a_j} \in [0, 1] / i, j = 1,2,..., n\}$$

$$[B] = \{\mu_{b_i b_j} \in [0, 1] / i, j = 1,2,..., m\}$$

The matrix [A] picks up the incidence relations, which can be produced between each of the elements, which act as causes, and the matrix [B] does the same with the elements, which act as effects. Both [A] and [B] match up the fact that both of them are reflexive matrixes, in another way:

$$\mu_{a_i a_j} = 1 / i, j = 1,2,..., n$$

$$\mu_{b_i b_j} = 1 / i, j = 1,2,..., m$$

In addition, they are translated in the fact that one element, cause or effect, has a bearing on itself at the maximum presumption.

In contrast none of [A] or [B] are symmetric matrixes, that is:

$$\mu_{a_i a_j} \neq \mu_{a_j a_i} \; i, j = 1,2,..., n$$

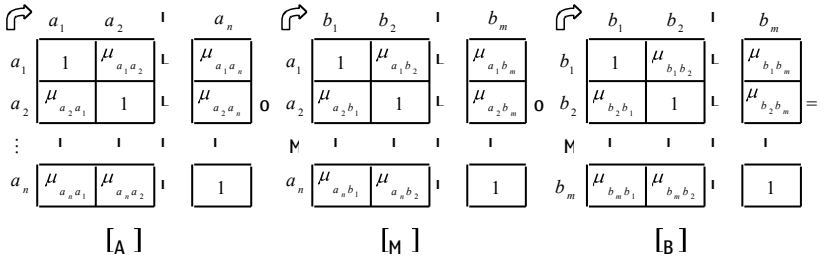
$$\mu_{b_i b_j} \neq \mu_{b_j b_i} \; i, j = 1,2,..., m$$

For obvious reasons.

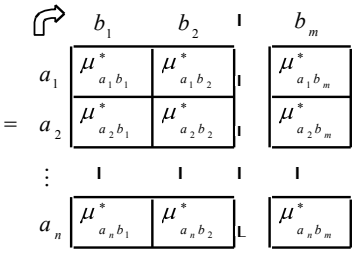
Once built the matrixes [M], [A] and [B] the establishment of all possible incidence (direct or indirect) combinations must be proceeded. To achieve it, we will realize the max-min composition of the three matrixes:

$$[A] \circ [M] \circ [B] = [M^*]$$

The obtained result will be a new matrix [M*] which picks up the incidences between causes and effects in second generation, in other words, the initial causal relations affected by the possible interposed incidence from a cause or effect.



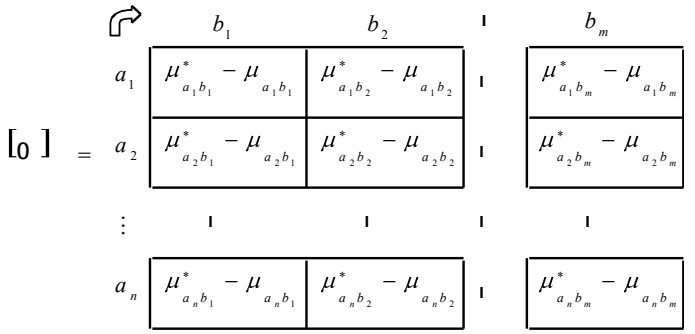
$$[A] \qquad [M] \qquad [B]$$



$$[M^*]$$

Therefore, the difference between the second-generation effects matrix and the direct incidence matrix will allow us to know the level in which some causality relations have been forgotten:

$$[O] = [M^*] (-) [M]$$



We must say, finally, that the higher the pertinence characteristic function value of the matrix [O] is, the higher is the forgotten level produced in the initial incidence relation. This is translated in the fact that the implications derived from some incidences not considered or taken into account in its fair intensity, can lead to mistaken decisions or not well estimated.

3. A medical diagnostic approach. The case of the Hereditary Hemochromatosis

In the medical professional field, we often found ourselves in front of different diseases with common symptoms [1-5,8-12]. Sometimes, the symptoms are so similar that we can even mistake the diseases. When a patient comes to a surgery, he/she describes several nuisances he/she suffers, which can be initial signs from different diseases, sometimes-distant diseases with very different prognostics. In this context, trying to establish links between symptoms and diseases with classical models based in probability is not an infallible guarantee in the diagnosis. Every symptom is subjective in every patient, and so is his/her perception and feeling of pain and the way they describe it to the doctor. That is why objective tests (such as blood analysis or radiographies) and subjective estimations (being able to explain a certain level of pain, pills effect or possible allergies) are used. Only this way it is possible to obtain the whole incidence relations and the relation level.

We will start the Forgotten Effects Model application statement showing two groups of elements, which will act as causes and effects. Note that the forgotten effects model is based on the concept of fuzzy relations [14], which is based on the notion of fuzzy sets [13,15-16]. We will call causes several diseases which could be suffered by a patient, and we will call effects the different symptoms which can be cause by the diseases. The main aim is the possibility of detecting a disease by a single symptom or group of different symptoms from the usual ones, simply because a symptom can happen to be at the same time, symptom of another symptom. We will show the mechanisms which can bring the hidden processes recuperation and we will study the incidence level in which can be produced.

Causes (diseases which could cause confusion):

a_1 = Hereditary Hemochromatosis (100%)
a_2 = Arthritis (30-40%)
a_3 = Cirrhosis (60%)
a_4 = Diabetes (50-60%)
a_5 = Fibrosis (60%)

Effects (symptoms caused):

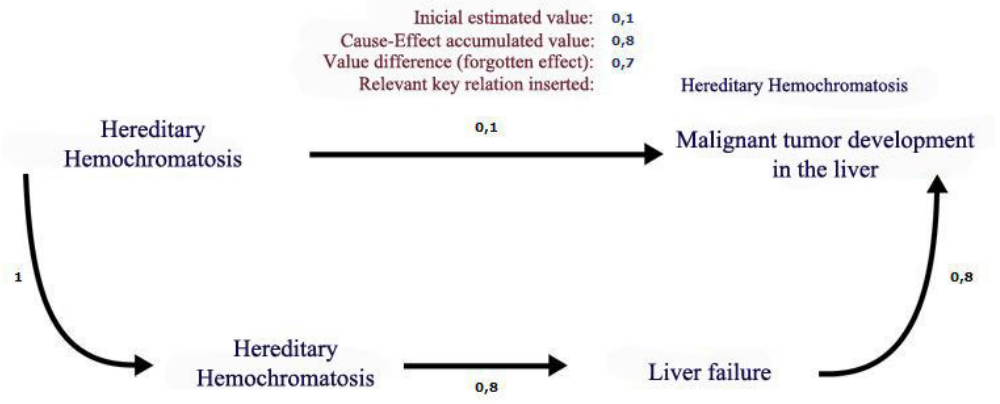
b_1 = Ferrous accumulation in the pituitary glands (15-35%)
b_2 = Testicular atrophy (15-35%)
b_3 = Weakness and tiredness (70-80%)
b_4 = Thyroid dysfunction (15-35%)
b_5 = Stomachache (60%)
b_6 = Hiperresonance to percussion (10%)
b_7 = General darkening of the skin (70%)
b_8 = Heart failure, arrhythmia and angina pectoris (20-30%)
b_9 = Pancreas failure (50-60%)
b_{10} = Liver failure (80%)
b_{11} = Rare noises in the respiratory tract (40%)
b_{12} = Increase of the bacterial infection risks (80%)
b_{13} = Suprarenal gland damage (15-35%)
b_{14} = Diarrhea (10%)
b_{15} = Sexual desire loss (15-35%)
b_{16} = Body hair loss (70%)
b_{17} = Weight loss (50%)
b_{18} = Increase of the thorax diameter (20%)
b_{19} = Fever (40%)
b_{20} = Malignant tumor development in the liver (5%)
b_{21} = Rash and pimples (60%)
b_{22} = Pain, inflammation and stiffness in the joints (30-40%)
b_{23} = Nasal polyps (20%)
b_{24} = Purulent nasal secretions (30%)
b_{25} = Warmness in the joints (30-40%)
b_{26} = Jaundice (70%)

b_{27} = Increase of the liver volume (50-60%)
b_{28} = Ascites (60%)
b_{29} = Digestive haemorrhage (40%)
b_{30} = Encephalopathy (conscience alterations, sleep disorders, confusion, mood changes) (85%)
b_{31} = Impotence (15-35%)
b_{32} = Menstruation disorder and/or early menopause (15-35%)
b_{33} = Varicose veins appearance (70%)
b_{34} = Increase of the parotid glands' size (15-35%)
b_{35} = Polydipsia, polyphagia and polyuria (15-35%)
b_{36} = Steatorrhea (70%)
b_{37} = Sickness and vomiting (45%)
b_{38} = Hypersensitivity in the paranasal womb (15%)
b_{39} = Blurry vision (40%)
b_{40} = Long cicatrisation of the wounds (50-60%)
b_{41} = Numbness and frequent tingling on hands and feet (50-60%)
b_{42} = Dry skin (70%)
b_{43} = Frequent haemoptysis (40%)
b_{44} = Intestinal obstruction (70%)

Matrix [M*]

Forgotten effects table $[O] = [M^*](-)[M]$

	E_1	E_2	E_3	E_4	E_5	E_6	E_7	E_8	E_9	E_{10}	E_{11}	E_{12}	E_{13}	E_{14}	E_{15}	E_{16}	E_{17}	E_{18}	E_{19}	E_{20}	E_{21}	E_{22}	E_{23}	E_{24}	E_{25}	E_{26}	E_{27}	E_{28}	E_{29}	E_{30}	E_{31}	E_{32}	E_{33}	E_{34}	E_{35}	E_{36}	E_{37}	E_{38}	E_{39}	E_{40}	E_{41}	E_{42}	E_{43}	E_{44}
C_1	0	0	0	0,2	0,7	0	0,1	0	0	0,2	0,2	0	0	0,6	0,5	0	0,1	0,4	0,4	0,7	0,2	0,3	0,4	0,3	0,3	0,1	0	0,2	0,2	0	0,4	0,3	0,2	0,3	0	0,4	0,4	0,1	0	0	0	0	0
C_2	0	0	0	0	0,5	0	0	0	0	0	0	0	0	0,5	0,8	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0,8	0	0,2	0	0	0	0,4	0	0,3	0	0,1	0,4	0,4	0	0
C_3	0	0	0	0,2	0,8	0,1	0,4	0	0,8	0,7	0,4	0,8	0	0,7	0,8	0	0	0,9	0,7	0,3	0,2	0,6	0,7	0,7	0,4	0	0	0	0	0	0	0	0	0	0,7	0	0,7	0,4	0,5	0,5	0,4	0,4	0,7	0
C_4	0,2	0	0,1	0,3	0,2	0,1	0,1	0,1	0,1	0,2	0,1	0,2	0	0,7	1	0,8	0	0	0,8	0,1	0,7	0,6	0,1	0,5	0,6	0,2	0,1	0,2	0,1	0,8	0	0	0,4	0	0,1	0	0,4	0	0	0	0	0,4	0,5	0,8
C_5	0	0	0	0	0	0	0,4	0	0	0	0	0,8	0	0	0,7	0	0	0	0,7	0	0	0	0	0	0	0	0	0	0,2	0,8	0	0	0	0	0	1	0	0	0	0	0	0,6	0	0



Matrix [O]

Taking back all the information in the model, general talking, we obtain two kinds of very valuable information for our aim in this research work.

At first place, if we take a look to the information of the matrix [M], which is the one who links the symptoms with the diseases (effects linked to causes), it is showed that there are four symptoms (which are the increase of the bacterial infection risk, the digestive haemorrhage, menstruation disorder and/or early menopause and Steatorrhea) which are the causes of a lot more symptoms directly linked with other diseases showed before. This can cause real

problems in the medical diagnosis, due to the confusion the doctor makes when he does not know if they are primary symptoms or symptoms caused by other symptoms. In this research work, we have made a process, which makes it able to untie the primary symptoms form the secondary ones, and this is a great step for the diagnosing system.

If we continue the analysis from the followed process and we take a look on the matrix [M*], we can observe that this matrix procures the real relation between one of the five crossed diseases (named causes) and the crossed accumulated symptoms which are produced. These diseases are extremely linked because the hereditary Hemochromatosis causes Arthritis, Cirrhosis, Diabetes and Fibrosis. The interaction between these five diseases is showed in the matrix [A].

The matrix [M*] proposes a real effect measured between 0 and 1 from the analysed diseases on the symptoms they cause, considering the crossed and accumulated effect of possible interactions between the variables which constitute the rows and columns. We can observe that the detection of a Hemochromatosis and the detection of a possible cirrhosis or possible diabetes through their symptoms would result basic for the early diagnosis of hereditary Hemochromatosis. This consideration comes from the high values which are observed in the matrix [M*].

This matrix acquires the highest relevance because it expresses the level with which a specific disease can cause different specific symptoms. These results are extremely important because they will be used by the medical facultative to establish necessary actuation protocols for the diagnosis and treatment of the hereditary Hemochromatosis. For example, if a patient is presented to the practitioner suffering from symptoms such as: testicular atrophy, liver failure, sexual desire loss, weight loss, fever, rash and pimples, pain, inflammation, warmness and stiffness in the joints and encephalopathy, he has 87% possibilities to suffer from Arthritis and a 26% conditional possibility that this Arthritis is caused by a hereditary Hemochromatosis.

To arrive to this conclusion we have selected the levels from the symptoms which are 0.8 or higher (80%) which show Arthritis (C_2 row) from the matrix [M*]. The reason why we have taken the higher levels is because when a patient goes to the doctor, he/she normally tells about the most signifying symptoms suffered, forgetting the less important ones, in this way, the symptoms which can cause Arthritis and don't overpass the 50% of incidence haven't been considered.

The model used in this research work concludes obtaining the matrix [O], also called forgotten effects matrix. It is the one, which gives us the information about the causality relations, which are not considered at diagnosing. The information contained in this matrix is maybe the most important, because it reminds us about symptoms, which are not taken into, account normally. The values in the matrix [O] represent the forgotten level that we have incurred at making the initial causality relation. In other words; the more careful the symptom-disease valuation will be made, the lower the forgotten levels will be. On the other side, the more things we will forget in the first step, and the higher the forgotten levels will appear. To sum up, this matrix [O] shows the symptoms, which have the risk to not being taken into account and not being linked to the disease.

To show how this method works, we have raised the interactions to one of the matrix [O] elements. This relation represents the followed process and shows that the brought element, which causes that an apparently insignificant incidence, could drag indirect and accumulated effects. Therefore, we observe that, initially, there was not any symptomatology relation between suffering hereditary Hemochromatosis and malignant tumor development in the liver. The model used shows that the relation is connected through the liver failure. That is because Hemochromatosis causes liver failure, and liver failure causes malignant tumors. Initially, the incidence of the tumors being caused by Hemochromatosis is only a 10%, but the forgotten effect rises up to an 80%.

This approach allows choosing symptoms, which show significantly a specific disease. The results help to make an early detection of a hidden disease through indirect symptoms. It is clear that the individual causality relations cannot solve the diagnosis problem, but analysing them together, we could make an advanced analysis of diseases with a difficult detection, even diseases hidden by other diseases.

The most important symptoms we should look to diagnose the hereditary Hemochromatosis would be sickness and vomiting, fever, impotence, weight loss, encephalopathy, body hair loss, sexual desire loss, stomach ache, weakness and tiredness.

Some of these symptoms are usually considered by the doctors at making the first diagnostics, but we can find ourselves in a situation where, for example, sexual desire loss or weakness and tiredness are not specific symptoms directly linked to the hereditary Hemochromatosis. Otherwise, if we add them to the rest of the symptomatology, they appear closely linked. This is why it is important for the doctors to have an actuation protocol starting from the elaboration of lists of common symptoms from different diseases hard to detect, in order to discover this kind of

affections as soon as possible.

4. Discussion

This research work pretends to get to know all the linked symptomatologies which can be showed Emergent and Rare diseases through mathematical models. It will allow us to know the disease in all its phases and start the treatment as soon as possible. These uncommon diseases shows up in the late stages of the patient's life, has quite ineffective treatments and its research has not been well funded. On the other hand, the problems in the diagnosis are caused by the similarity between its symptoms and other diseases' symptoms. We tackle a mathematic model which can solve the early diagnosis and, as consequence, the earlier treatment. It is based in a searching process, which links different symptoms caused by different diseases with a common origin. The calculations obtained allow us to distinguish groups of symptoms which, raised together, allow us to detect a specific disease and reject other diseases, which could cause confusion while diagnosing. In summary, the mathematical models are useful to make an early and correct diagnostic without the need to make any genetic test or waiting for the late symptoms to appear.

A better study of REDs will allow determining the type, form and stage of the disease in the short term. This will allow in the medium and long term, to diagnose corresponding rare diseases in order to prevent development of the disease in a more complex shape for the diagnosis, follow-up laboratory studies, as well as deaths.

The research and innovative spillovers are intended to develop in two major stages. The first stage led by our pioneering medical team attends all the phases in the process of early diagnostics and treatment of rare and emergent diseases such as appearance, evolution and forecast, as well as their medical implications. The second stage led by the conjunct efforts of our engineering and economic teams consists in a profound analysis on the economic and financial consequences that the mentioned diseases have on UE health systems. The final objective of the research is to reach sustainable long-term wellbeing of the population, specifically the stages are:

i. Improve the early diagnosis utilizing computing techniques and treatment of the information, so the people affected do not only get a longer life expectancy, but also an improved quality of life, while saving resources to the public finances. The pretended research has its foundation on an exhaustive study of the common protocols in detection of rare and emergent diseases, putting special emphasis on some particular cases. A study on real life challenges and obstacles in the diagnostic process to patients presenting rare diseases it has also planned to be conducted. An exhaustive study comparing the existing situation in the EU, countries' surrounding the EU and developing countries is going to be made. Then, both technical and economic analysis will be led to improve the medical diagnostic protocols, saving time in the detection of rare diseases and accelerating the treatment, in case there is. These improvements will rely on application of computation techniques based on hybrid information systems, which combine numeric and non-numeric analysis. The innovative idea is to facilitate the creation of simple computing programs for personnel who treat the patients at a first instance. To detect and refer a patient in an adequate and efficient way results as high priority for society and the general wellbeing of the population.

ii. The second target of this research focus on the economic calculation and the savings that the early diagnose of rare diseases represent for the public health system and the patients. Effective diagnostics turn out in direct or indirect cost reduction. In order to complete that task, a field study will be carried out focusing on the next issues:

   - Public Health:
     1. Development of new tests or protocols utilizing new information technologies that their cost is null or residual.
     2. Reduction on the number of admissions or time spent in hospitals due to the efficiency on the diagnostics.
     3. Reduction on the number of medical consults, eliminating duplicate tests or repetitive specialists refers.
     4. Reduction on the number of diagnostic trials, suppressing duplicities and repetition due to the delay in diagnostics.
     5. With an effective diagnose, the patients could improve their quality of life, and still be part of the active population.
   - Labour Costs:

1. Correct utilization of medical insurance and the reduction of costs for the labour assurances.
2. Reduction on costs for work absence due to repetitive visits to health facilities.

- Quality of life:
  1. Better conditions for the patients. Early treatment supposes better conditions and life expectancy.
  2. Reduction on personal and familiar costs due to treatment, therapies, diagnostic trials, etc.
  3. Reduction on dependency costs, providing early diagnose means better quality of life.
  4. Reduction on visits and consults to health facilities, therefore decreasing work absence.

Appendix A. An example appendix

Incidence table between the different effects [B]

	E_1	E_2	E_3	E_4	E_5	E_6	E_7	E_8	E_9	E_{10}	E_{11}	E_{12}	E_{13}	E_{14}	E_{15}	E_{16}	E_{17}	E_{18}	E_{19}	E_{20}	E_{21}	E_{22}	E_{23}	E_{24}	E_{25}	E_{26}	E_{27}	E_{28}	E_{29}	E_{30}	E_{31}	E_{32}	E_{33}	E_{34}	E_{35}	E_{36}	E_{37}	E_{38}	E_{39}	E_{40}	E_{41}	E_{42}	E_{43}	E_{44}
E_1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0,8	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
E_2	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0,2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0,2	0	0	0	0	0	0	0
E_3	0,8	1	1	0	0	0	0,8	0	0	0	0	0	0	0	0,8	0	0	0	0	0	0	1	0	0	0,9	0	0	0	0	1	0,8	1	0	0	0	0	0	0	0	1	0	0	0
E_4	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0,6	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E_5	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E_6	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E_7	0	1	0	0,4	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0,5	0,5	0	0	0	0	0	0,5	0	0	0	0	0	0	0	0
E_8	0	1	0	1	0	0	0	1	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	1	0	1	0,4	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0
E_9	0	1	0	1	0	0	0	0	1	0	0	0	0	0,7	0	0	0	0	0	0,8	1	0	0	0	0	1	0	1	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0
E_{10}	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0,4	0	0
E_{11}	0	1	0	1	0	0	0	0	0	0	1	0	0	1	0	0	0	0	1	0	0	1	0	0	0,9	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0
E_{12}	0,2	1	0,1	0,2	0,2	0,1	0,1	0,1	0,1	0,2	0,1	1	0	0,6	0	0	0,4	0	1	0,1	0,3	0,6	0,1	0,5	0,6	0,2	0,1	0,2	0,1	0,7	0,2	0,2	0,4	0	0,1	0,7	0,4	0	0	0	0,1	0,4	0,2	0
E_{13}	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0,8	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
E_{14}	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E_{15}	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E_{16}	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E_{17}	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E_{18}	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E_{19}	0	1	0	0	0,5	0	0	0	0	0	0	0	0	0,5	0,8	0	0	0	1	0	0,5	0,4	0	0	0	0	0	0	0	0,8	0	0,2	0	0	0	0,4	0	0,3	0	0,1	0	0	0
E_{20}	0	1	0	0	0	0	0	0	1	0	0	0	0	0,4	0	0	1	0	0,1	1	0,4	0	0	0	0	0,8	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0,3	0	0	0
E_{21}	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0,4	0	0	0
E_{22}	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E_{23}	0	0,1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0,2	0	0	0	1	1	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0
E_{24}	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0,3	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
E_{25}	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E_{26}	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E_{27}	0	0,5	0	0,8	0	0,1	0	0	0,8	0	0	0	0	0	0	0	0,5	0,9	0	0,3	0	0	0	0	0	0,5	1	0	0	0	0	0	0	0	0,5	0	0	0	0	0,1	0	0	0
E_{28}	0	0,9	0	1	0	0	0	0	0	0	0,4	0,8	0	0	0,1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0,1	0
E_{29}	0	1	0	1	0	0	0,4	0	0	0	0	0,8	0	0,7	0,6	0	0,3	0	1	0	0	0	0	0	0	0	0	0	1	0	0	0,2	0	0	0,4	1	0	0,2	0,5	0,5	0	0,4	0,7	0
E_{30}	0	1	0	0	0,8	0	0	0	0	0	0	0	0	0,7	0	0,6	0	0,6	0	0	0	0	0	0	0	0	0	0	0	1	0	0,5	0	0	0	0,1	0	0,4	0	0	0	0	0	0
E_{31}	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
E_{32}	0	1	0	0	0	0	0,1	0	0	0	0	0	0	0,7	0,8	0,4	0	0	0	0,2	0,6	0	0	0,4	0	0	0	0	0,6	0	1	0	0	0	0,2	0	0	0	0	1	0	0	0,8
E_{33}	0	0,7	0	0	0,6	0	0	0	0	0	0	0,9	0	0	0	0	0	0	1	0	0,1	0	0	0	0	0	0	0	0,4	0	0	1	0	0	0	0,6	0	0	0	0	0	0	0	0
E_{34}	0	0,2	0	0	0	0	0	0	0	0	0	0	0	0,3	0	0	0	0	0	0	0,2	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0,5	0
E_{35}	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
E_{36}	0	1	0	1	0,2	0	0,1	0	0	0	0	0	0	0,7	1	0	0,8	0	0,7	0	0,2	0	0	0	0	0	0	0	0,6	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
E_{37}	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0,4	0,4	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0
E_{38}	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0,8	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
E_{39}	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
E_{40}	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
E_{41}	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0,7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0,6	0	1	0	0
E_{42}	0	1	0	0,8	0	0	0	0	0	1	0	0,9	0	0	0,2	0	1	0	1	0	0	0	0	0	0	0	0	0	0,7	0	0	0	0	0	0,1	0	0	0	0	0	0	0	0	0
E_{43}	0	1	0	1	0	0	0,4	0	0	0	0	0,6	0	0	0,7	0	0	0	0	0	0	0	0	0	0	0	0	0	0,2	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0
E_{44}	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1

Matrix [B]

Estimated incidences table between causes and effects $(\underset{\sim}{M})$

	E_1	E_2	E_3	E_4	E_5	E_6	E_7	E_8	E_9	E_{10}	E_{11}	E_{12}	E_{13}	E_{14}	E_{15}	E_{16}	E_{17}	E_{18}	E_{19}	E_{20}	E_{21}	E_{22}	E_{23}	E_{24}	E_{25}	E_{26}	E_{27}	E_{28}	E_{29}	E_{30}	E_{31}	E_{32}	E_{33}	E_{34}	E_{35}	E_{36}	E_{37}	E_{38}	E_{39}	E_{40}	E_{41}	E_{42}	E_{43}	E_{44}
C_1	0,2	0,8	0,2	0,6	0,1	0,7	0,3	0,5	0,8	0,4	0,2	0,8	0,2	0,1	0,2	0,7	0,5	0,2	0,4	0,1	0,6	0,3	0,2	0,3	0,3	0,7	0,6	0,6	0,4	0,8	0,2	0,3	0,2	0,2	0,7	0,4	0,2	0,4	0,6	0,5	0,7	0,4	0,7	0,7
C_2	0	1	0	0	0	0	0	0	0	0,8	0	0	0	0	0	0	0,8	0	0,8	0	0,8	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
C_3	0	1	0	0,8	0	0	0	0	0	0	0	0	0	0	0	0,8	1	0	0	0	0	0	0	0	0	1	1	1	0,6	1	0,8	0,6	0,1	0	0	0,8	0	0	0	0	0,2	0	0	0,8
C_4	0	1	0	0,7	0	0	0	0	0	0	0	0,8	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0,8	0,8	0	1	0	1	0	0,8	1	0,9	0,8	0	0	0
C_5	0	1	0	1	0,7	0	0	0	0	0,9	0	0	0	1	0	0	0,9	0,8	0	0	0	0	0,8	1	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0,7	1	0

Matrix [M]

Incidence table between the different causes $(\underset{\sim}{A})$

	C_1	C_2	C_3	C_4	C_5
C_1	1	0,3	0,6	0,5	0,6
C_2	0	1	0	0	0
C_3	0	0	1	0	0,7
C_4	0	0	0	1	0
C_5	0	0	0	0	1

Matrix [A]

Max-min convulation table between the matrixes $(\underset{\sim}{A})\circ(\underset{\sim}{M})\circ(\underset{\sim}{B}) = (\underset{\sim}{M}^*)$

	E_1	E_2	E_3	E_4	E_5	E_6	E_7	E_8	E_9	E_{10}	E_{11}	E_{12}	E_{13}	E_{14}	E_{15}	E_{16}	E_{17}	E_{18}	E_{19}	E_{20}	E_{21}	E_{22}	E_{23}	E_{24}	E_{25}	E_{26}	E_{27}	E_{28}	E_{29}	E_{30}	E_{31}	E_{32}	E_{33}	E_{34}	E_{35}	E_{36}	E_{37}	E_{38}	E_{39}	E_{40}	E_{41}	E_{42}	E_{43}	E_{44}
C_1	0,2	0,8	0,2	0,8	0,8	0,7	0,4	0,5	0,8	0,6	0,4	0,8	0,2	0,7	0,7	0,7	0,6	0,6	0,8	0,8	0,8	0,6	0,6	0,6	0,6	0,8	0,6	0,8	0,6	0,8	0,6	0,6	0,4	0,5	0,7	0,8	0,6	0,5	0,6	0,5	0,7	0,4	0,7	0,7
C_2	0	1	0	0	0,5	0	0	0	0	0,8	0	0	0	0,5	0,8	0	0,8	0	0,8	0	0,8	1	0	0	1	0	0	0	0	0,8	0	0,2	0	0	0	0,4	0	0,3	0	0,1	0,4	0,4	0	0
C_3	0	1	0	1	0,8	0,1	0,4	0	0,8	0,7	0,4	0,8	0	0,7	0,8	0,8	1	0,9	0,7	0,3	0,2	0,6	0,7	0,7	0,4	1	1	1	0,6	1	0,8	0,6	0,1	0	0,7	0,8	0,7	0,4	0,5	0,5	0,6	0,4	0,7	0,8
C_4	0,2	1	0,1	1	0,2	0,1	0,1	0,1	0,1	0,2	0,1	1	0	0,7	1	0,8	1	0	0,8	0,1	0,7	0,6	0,1	0,5	0,6	0,2	0,1	0,2	0,1	0,8	0,8	0,8	0,4	1	0,1	1	0,4	0,8	1	0,9	0,8	0,4	0,5	0,8
C_5	0	1	0	1	0,7	0	0,4	0	0	0,9	0	0,8	0	1	0,7	0	0,9	0,8	0,7	0	0	0	0,8	1	0	0	0	0	0,2	0,8	0	0	0	0	1	1	1	0	0	0	0	0,4	1	0

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